IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:			
Andrey A. BOUKHAROV *et al.*		Art Unit:	1631
Appln. No.:	09/620,392	Examiner:	S. ZHOU
Filed:	July 19, 2000	Atty. Docket:	16517.112
For:	Plant Genome Sequences and Uses Thereof		

#22
Plunkett
10/7/02
1663

APPELLANT'S BRIEF

Commissioner for Patents
Washington, DC 20231

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-described patent application. A Notice of Appeal was filed on July 1, 2002. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter. *This Brief is submitted in triplicate.*

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

The Appellant is unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 1-4, 6-9 and 16-20 are pending. Claims 1-4, 6-9 and 16-20 stand finally rejected under 35 U.S.C. §§ 101 and 112, first paragraph. Claims 1-2 and 17-18 also stand finally rejected under 35 U.S.C. § 102. Applicants appeal all of the rejections of claims 1-4, 6-9 and 16-20.

4. Status of Amendments

Applicants have filed three Amendments subsequent to the Final Office Action mailed March 1, 2002 (Paper Number 15) ("Final Action"), in this case. The Amendment and Reply dated June 3, 2002, has been partially entered, per the Advisory Action mailed on June 21, 2002 (Paper No. 17) ("First Advisory Action"). The proposed amendments to the claims were not entered because they allegedly would "raise new issues that would require further consideration and/or search". First Advisory Action at pages 1-2.

Applicants proceeded to file an Amendment After Final Rejection by facsimile on September 10, 2002. After a conference with the Examiner on September 12, 2002, it is Applicants' understanding that the proposed amendments filed in the Amendment After Final Rejection of September 10, 2002, were not entered. Applicants proceeded to file a Second Amendment After Final Rejection by facsimile on September 12, 2002. It is Applicants' understanding that the Examiner entered the proposed amendments filed in the Second Amendment After Final Rejection, as reflected in the Advisory Action mailed September 19, 2002 (Paper Number 20) ("Second Advisory Action").

5. Summary of Invention

The invention is directed to substantially purified nucleic acid molecules having a nucleic acid sequence of SEQ ID NO: 1, and to substantially purified nucleic acid molecules having between 90% and 100% sequence identity with a nucleic acid molecule having the sequence set forth in SEQ ID NO: 1 or complement thereof. Specification at page 12, lines 13-20. The

invention is also directed to substantially purified nucleic acid molecules comprising from about 50 to about 100 nucleotide residues of the nucleic acid sequence set forth in SEQ ID NO: 1, specification at page 12, lines 13-24, and to purified nucleic acid molecules comprising from about 50 to about 100 nucleotide residues, where the nucleic acid molecule exhibits complete complementarity to a fragment of a second nucleic acid molecule having the nucleic acid sequence of SEQ ID NO: 1 or complements thereof. *Id.*

6. Issues

The issues in this Appeal are:

(a) whether claims 1-4, 6-9 and 16-20 are unpatentable under 35 U.S.C. § 101 for allegedly being unsupported by a specific asserted utility or a well established utility;

(b) whether claims 1-4, 6-9 and 16-20 are unpatentable under 35 U.S.C. § 112, first paragraph for alleged lack of enablement because the claimed invention purportedly lacks utility;

(c) whether claims 1-4, 6-9 and 16-20 are unpatentable under 35 U.S.C. § 112, first paragraph for alleged insufficiency of written description;

(d) whether claims 1-4, 6-9 and 16-20 are unpatentable under 35 U.S.C. § 112, first paragraph for alleged lack of enablement because undue experimentation would supposedly be required to use the claimed nucleic acid molecules; and

(e) whether claims 1-2 and 17-18 are unpatentable under 35 U.S.C. § 102 for alleged anticipation.

7. Grouping of Claims

Claims 1-4, 6-9 and 16-20 remain in this case. Claims 1, 2, 16 and 17 are independent, and they do not stand or fall together. The patentability of these claims, and claims depending therefrom, is addressed in Sections 8.A through 8.F below. A copy of the currently pending claims is attached hereto as Appendix A.

8. Argument

A. Summary of Appellant's Position

As the Supreme Court said in *Brenner v. Manson*, the "basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility....where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Applicants have met their part of the bargain – they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example, the ability to identify the presence or absence of a polymorphism in a population of rice plants. This benefit is specific, not vague or unknown, and it is a "real world" or substantial benefit. Because the claimed nucleic acid molecules provide at least this benefit, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed nucleic acid molecules for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Furthermore, Applicants have provided an adequate description of the claimed nucleic acid molecules that demonstrates Applicants' possession of the claimed invention. The genera of claimed nucleic acid molecules, *e.g.,* the genus of nucleic acid molecules comprising the nucleic acid sequence of SEQ ID NO: 1 of claim 1, have been described by the recitation of common structural features, *e.g.,* the nucleotide sequence of SEQ ID NO: 1, which distinguishes molecules in the claimed genera from molecules not in the claimed genera. Because the specification demonstrates that Applicants had possession of (and have provided an adequate description of) the claimed genera of nucleic acid molecules, the specification satisfies the written description requirement of 35 U.S.C. § 112.

Applicants have asserted that the claimed nucleic acid molecules actually work for that and other utilities disclosed and described in the specification, and so both enablement rejections

must be reversed. Applicants have asserted that one skilled in the art is able to use the claimed nucleic acid molecules for at least two disclosed utilities, namely use to identify the presence or absence of a polymorphism and use as a hybridization probe for expression profiling. *See, e.g.,* specification at page 57, line 3 through page 64, line 4 and page 64, lines 5-12. The law clearly establishes that the enablement requirement is satisfied if at least one mode of making and using the invention is enabled. Because Applicants have asserted that the claimed nucleic acid molecules work for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Claims 1, 2, 17 and 18 were erroneously rejected as anticipated by a reference which not only is not prior art under 35 U.S.C. § 102(b), but which also fails to teach any of the recited nucleic acid sequences. The Examiner improperly considered non-identical chemical compounds to anticipate the claims, despite the fact that the reference fails to teach the chemical composition of SEQ ID NO: 1 or its complement. Moreover, the rejections are not based on what exists in the art or what the art teaches, but rather on the Examiner's theory, unsupported by any evidence, that the art sequence might anticipate the claims if certain claim limitations were interpreted contrary to the teachings of the specification. Such clearly unsupported conjecture is simply not a proper basis for an anticipation rejection.

B. The Claimed Nucleic Acid molecules Have Legal Utility

Pending claims 1-4, 6-9 and 16-20 were erroneously rejected under 35 U.S.C. § 101 because the claimed inventions were allegedly not supported by either a "specific, substantial, and credible utility or, in the alternative, a well-established utility." Final Action at page 3. Furthermore, the Examiner reiterates this rejection in the First Advisory Action by declaring that the asserted utilities, for example, of probing for a particular gene or detecting the presence or absence of a polymorphism, are "not specific to the claimed invention" and not substantial

"because further research is needed to determine a specific, substantial and credible utility for the possible polymorphisms detected". First Advisory Action at page 2.

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

The courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Applicants have asserted in the specification that the claimed nucleic acid molecules provide identifiable benefits, for example, use to identify the presence or absence of a polymorphism, and use as a hybridization probe for expression profiling. *See, e.g.*, specification

at page 57 line 3 through page 64, line 4, and page 64, lines 5 through 12. Either of these utilities described alone is enough to satisfy Section 101. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

1. The Claimed Nucleic Acid Molecules Provide A Specific Benefit, *i.e.*, They Have Specific Utility

The Examiner acknowledges that the instant specification describes multiple utilities for the present invention, including use of the nucleic acid molecules "for gene mapping, marker assisted introgression of traits, physical mapping, etc." Office Action mailed September 25, 2001 (Paper Number 12), at page 6. In addition, the specification also discloses additional utilities for the claimed nucleic acid molecules,[1] including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide or traits such as protein synthesis activity. Specification at page 69, lines 7 through 20 and at page 86, line 11 through page 88, line 24. For example, a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored. Such a screen is analogous to a cell-based assay, which has a legally sufficient utility.[2] Other utilities disclosed in the specification include use of the claimed nucleic acid molecules to measure the level of mRNA in a sample,[3] and use as molecular markers.[4]

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[1] It is irrelevant whether the corresponding mRNA or polypeptide have utility because Applicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules.

[2] *See, e.g.*, MPEP § 2107 at page 2100-32.

[3] It is standard practice to screen populations of nucleic acids with EST sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, drought stress. Contrary to the Examiner's assertions, this use is not using the claimed nucleic acid molecules to identify a "'real world' context of use." *See* Office Action mailed September 25, 2001, at page 5. It is a **use** of the claimed nucleic acid molecules in a real world context.

(a) Identifying the Presence or Absence of a Polymorphism

One of the utilities disclosed in the specification is use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism. Specification at page 57, line 3 through page 64, line 4. The Examiner argues that this utility, like all of the asserted utilities, is not specific or substantial, *see* Final Action at pages 3-4, First Advisory Action at page 2, but does not provide any support (legal or factual) for the proposition that detection of polymorphisms is not a legal utility.

Many of the disclosed utilities in this case, including the detection of polymorphisms, are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The Examiner denigrates such utilities by asserting that these utilities are not "useful" because they "are generic to any rice nucleic acid sequences." *See* Final Action at page 3. However, the fact that, for example, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107 at page 2100-33.

Use of the claimed nucleic acid molecules to detect the presence or absence of polymorphisms is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical

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[4] One can use the claimed nucleic acid molecules to determine location of a corresponding DNA sequence on a physical map or genetic map location without knowing anything beyond the claimed sequence. The use of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits.

element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[5] Likewise, the claimed nucleic acid molecules have utility even if, for example, the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usefully demonstrates that the two (or more) populations being compared share a common genetic heritage.

The claimed nucleic acid molecules have been asserted to work for a specific, *i.e.*, not vague or unknown benefit – to identify the presence or absence of a polymorphism. This benefit is immediately realized directly from the use of the claimed nucleic acid molecules, not from the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Probes for Other Molecules or Source for Primers

Other uses for the claimed nucleic acid molecules are as probes for other molecules and as a source of primers. The Examiner suggests that these uses are not legal utilities because "probing for a gene is not specific to the claimed invention". First Advisory Action at page 2. This is not correct. The specification discloses that the claimed nucleic acid molecules can be used, via hybridization, in real world applications such as to isolate nucleic acid molecules of other plants and organisms such as alfalfa, *Arabidopsis*, barley, *Brassica*, cotton, maize, peanut, etc.[6] Specification at page 34, lines 9 through 21. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and so has not met the burden of proof

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[5] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

[6] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Applicants to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules.

required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

One illustrative example of a molecule that can be isolated using a claimed nucleic acid molecule is the promoter of the gene corresponding to that claimed nucleic acid molecule. Applicants have specifically disclosed that one use of the claimed nucleic acid molecules is to initiate a chromosome walk. Specification at page 49, line 5 through page 51, line 24. The Final Action denigrates that utility when it asserts that it is a utility that is applicable to any rice nucleic acid sequence. Final Action at page 3, *see also* First Advisory Action at page 2.

In short, the Examiner suggest that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose, *i.e.*, chromosome walks. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not "specific" to the claimed nucleic acid molecules. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in *Oryza sativa*. A random nucleic acid molecule does not provide an equally good starting point to isolate such a

promoter. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules. An invention may be "less effective than existing devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed nucleic acid molecules could not be so used. Accordingly, the assertion of this utility as a probe for other molecules or as a source of primers satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

2. The Claimed Nucleic Acid Molecules Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also appears to assert that the disclosed uses are legally insufficient because they are not "substantial" utilities. Final Action at pages 3-4, First Advisory Action at page 2. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). " 'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[7]

There can be no question that one skilled in the art can use the claimed nucleic acid molecules in a manner which provides an immediate benefit to the public, *e.g.*, to detect the presence or absence of polymorphisms. The detection of polymorphisms provides an immediate

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[7] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

benefit to the public because, for example, it enables a plant breeder to determine the distribution of parental genetic material in the progeny of a cross. This information about a plant's genetic profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

Quite apart from the detection of polymorphisms, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to such nucleic acid molecules. The utility of ESTs is not merely an academic issue; the real world value of ESTs is self-evident from the growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs. Like fermentation processes involving bacteria, ESTs and nucleic acid molecules with EST sequences are "industrial product[s] used in an industrial process – a useful or technical art if there ever was one." *See, e.g., In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for EST products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Cf. Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) ("People rarely, if ever, appropriate useless inventions"). Quite simply, the commercial value of ESTs is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

3. The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in which utility was found not to be credible are rare, and usually involve "hare-brained"

utilities.[8] A challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107 at 2100-40.

Applicants have explicitly identified specific and substantial utilities, not only in the specification, but in Applicants' Response dated June 3, 2002, at page 6. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed nucleic acid molecules will not work for the disclosed utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of claims 1-4, 6-9 and 16-20 under 35 U.S.C. § 101 is improper and should be reversed.

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[8] Examples of incredible utilities are given in MPEP § 2107 at page 2100-34, and include:

> an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

C. The Claimed Nucleic Acids Are Enabled by the Specification

The enablement of the claimed nucleic acid molecules has been challenged. Claims 1-4, 6-9 and 16-20 were erroneously rejected under 35 U.S.C. § 112, first paragraph, as not enabled by the specification, because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled. Final Action at page 4, First Advisory Action at page 2. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

D. The Specification Provides An Adequate Written Description of the Claimed Invention

Despite the Examiner's admission that the specification describes SEQ ID NO: 1 (Office Action mailed September 25, 2001, at page 6), the adequacy of the written description has been challenged by the Examiner allegedly because "one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of DNAs or RNAs encompassed in claims 1-4, 6-9 and 16-20, which comprises the sequence of the claimed SEQ ID NO." Final Action at page 5. The basis for the Examiner's challenge is that "there is substantial variability among the species of the polynucleotides or nucleic acids encompassed within the scope of the claims. . . due to the use of the open language 'comprising' or 'having'." *Id.* This is not a proper basis for a written description rejection of a "comprising" claim. If it was, every "comprising"

claim ever written would be invalid for failing to describe every nuance of the claimed invention. Furthermore, the specification demonstrates to one skilled in the art that Applicants were in possession of the claimed genera of nucleic acid molecules.

1. The Specification Reflects Applicants' Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if every nuance of the invention was not expressly described, then the written description requirement has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. After reading the present specification, a person of ordinary skill in the art, *e.g.*, a molecular biologist, would understand that Applicants had possession of nucleic acid molecules comprising SEQ ID NO: 1 or complement thereof, or a fragment of either.

Applicants have provided the nucleotide sequence required by the claims, *i.e.*, SEQ ID NO: 1, as well as, for example, vectors comprising the nucleic acid sequence (*see, e.g.*, specification at page 69, line 7 through page 77, line 4), and bacterial artificial chromosomes (BACs) that comprise or are complementary to the nucleic acid sequence (*see, e.g.*, specification at page 19, lines 3-24). The fact that the claims at issue are intended to cover molecules that include the recited sequence joined with additional sequences, or that hybridize under specific conditions to the recited sequence does not mean that Applicants were any less in possession of

the claimed nucleic acid molecules.[9] It is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

The present application describes more than just the nucleotide sequence required by the claims (SEQ ID NO: 1). For example, it describes vectors comprising the claimed nucleic acid molecules (specification at page 69, line 7 through page 77, line 4), and describes how to make the nucleotide sequences and the libraries from which they were originally purified. *See* specification at page 3, line 4 through page 8, line 2, and Examples 1-3. Furthermore, the addition of extra nucleotides or detectable labels to the disclosed nucleotide sequence (SEQ ID NO: 1) is readily envisioned by one of ordinary skill in the art upon reading the present specification,[10] in particular at page 39, line 9 through page 40, line 8 (describing fusion peptide molecules encoded by the claimed nucleic acid molecules), page 21, line 11 through page 22, line 16 (describing the identification of microsatellites), page 67, line 23 through page 69, line 6 (describing site directed mutagenesis) and page 89, line 25 through page 90, line 5 (citing references describing the construction, manipulation and isolation of nucleic acid macromolecules). Moreover, it is well established that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570,

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[9] If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then it goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

[10] It is established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *E.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A.. 1981)).

2. Applicants Have Described the Claimed Invention

The Examiner asserts that because Applicants have not disclosed "any nucleic acid that minimally contains the sequence of the claimed SEQ ID NO, including any full length gene which contain the sequence, and fusion constructs, any RNAs or cDNAs, etc.", Applicants have allegedly not adequately disclosed the claimed genus. Office Action mailed September 25, 2001, at page 6. The Examiner appears to assert that each nucleic acid molecule within the claimed genus must be described by its complete structure. These assertions are totally unfounded. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Applicants have satisfied that test for written description.

In particular, Applicants have disclosed common structural features, for example, the nucleotide sequence of SEQ ID NO: 1. The respective common structural feature (the nucleotide sequence of SEQ ID NO: 1) is shared by every nucleic acid molecule in the claimed genus, and it distinguishes the members of the claimed genus from non-members. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 1, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1.[11] If a nucleic acid molecule does not contain SEQ ID NO: 1, then it is not a member of that claimed genus. The presence of other nucleotides at either end of the recited

[11] The same argument applies with equal force to variations of the claimed nucleic acid molecules. For example, one skilled in the art would readily recognize an mRNA including a nucleic acid molecule that has, *i.e.*, 95% sequence identity with SEQ ID NO: 1 as a member of the claimed genus. *See* claim 17.

sequence will not interfere with the recognition of a claimed nucleic acid molecule as such – it either contains the nucleotides of SEQ ID NO: 1 or it does not. On skilled in the art, after reading the present specification, would clearly know if a nucleic acid molecule contains one of the recited nucleotide sequences. Thus, claims 1-4, 6-9 and 16-20 are supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, and the rejection should be reversed.

E. The Specification is Enabling for the Scope of the Claimed Nucleic Acid Molecules

Claims 1-4, 6-9 and 16-20 were erroneously rejected as not being enabled by the specification. The Examiner admits that the specification is enabling for polynucleotides and nucleic acids of SEQ ID NO: 1, however, the Final Action asserts the specification "does not enable any person skilled in the art ...to make and use the invention commensurate in scope with these claims." Final Action at page 5.

The Examiner cites no support for the proposition that the full scope of the claims would require undue experimentation by one of ordinary skill in the art to make or use the claimed invention. Furthermore, in view of the Examiner's admission that SEQ ID NO: 1 is enabled, and the well established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques" (*see, for example, Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000)), which would include the use of the claimed nucleic acid sequences with other nucleic acid sequences, Applicants submit the Examiner has not met the required burden. Applicants further assert that the use of the transitional phrase "comprising" or "having", which leaves the claims "open for the inclusion of unspecified ingredients even in major amounts" (*Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48

U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986)) is well established in patent jurisprudence.

The First Advisory Action attempts to abrogate the Examiner's burden to present evidence that the claims are not enabled by arguing that "the claimed invention, i.e. nucleic acids comprising or having the sequence of the elected SEQ ID NO: 1 is a genus that contains a highly variable species." First Advisory Action at page 2. In response, Applicants submit that an analysis of the criteria presented by *In re Wands* supports Applicants' position that no undue experimentation would be required to make and use the claimed invention. *See In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1998).

The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, identification of an active site, and radiometric synthase assay conditions, to which a person of ordinary skill in the art has access. Performing routine and well-known steps, such as sequence alignment protocols, molecular weight determination, and antibody hybridization assays, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 218-219 (C.C.P.A. 1976).

The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. Again, the specification provides evidence of sequence identity, discloses start and stop positions within a sequence, and discusses the use of the claimed SEQ ID NO to isolate additional sequences within a genome. *See, e.g.,* Examples 1-3 and Table 1. Based on such disclosure, one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with the claims.

The fourth, fifth, and sixth *Wands* criteria focuses on the nature of the invention, the state of the art, and the relative skill in the art. The present invention relates to nucleic acid molecules comprising nucleic acid sequences, and the specification further describes amino acid sequences

derived therefrom, and constructs and methods related thereto. *See, e.g.*, specification at page 30, line 15 through page 40, line 8 (describing polypeptide molecules and homologues), and page 69, line 7 through page 86, line 15 (describing use of the claimed nucleic acid molecules in methods of transforming plants). Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to identify, confirm, and introduce into other hosts, nucleic acid and amino acid sequences.

The seventh criterion considers the predictability of the art. While the Final Action admits that the specification is "enabling for polynucleotides/nucleic acids of the elected SEQ ID NO: 1", the First Advisory Action alleges that this is not enabling for the full scope of the claims because "nucleic acids comprising or having the sequence of the elected SEQ ID NO: 1 is a genus that contains highly variable species." Final Action at page 5, First Advisory Action at page 2. Applicants respectfully disagree and assert, as discussed *supra*, that the specification discloses sufficient guidance to render the results of substitutions, additions, and deletions within the claimed SEQ ID NO predictable. *See, e.g.,* specification at page 32, line 18 through page 38, line 9.

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). In the present case, one of skill in the art is specifically guided by the disclosure to look to, *e.g.*, sequence identity data in making that determination.

The Examiner has presented no evidence supporting the allegation that one of ordinary skill in the art would not be able to make or use the claims nucleic acid molecules in light of Applicants' disclosure. Furthermore, the analysis of the Wands factors, discussed *supra*, conclusively establishes that one of ordinary skill in the art would be able to make and use the

claimed invention based on the disclosure in the specification. Accordingly, for at least these reasons, the enablement rejection under 35 USC § 112, first paragraph, is improper and must be reversed.

F. The Claimed Nucleic Acid Molecules Are Novel

The Examiner has challenged the novelty of the claimed nucleic acid molecules in the Final Action. Claims 1-2 and 17-18 were erroneously rejected under 35 U.S.C. § 102(b), for allegedly being anticipated by Birren, *et al.* (Genbank accession No. AC005922, November 14, 1998) (hereinafter "Birren"). Final Action at page 6.[12]

Birren does not anticipate the present claims. For a prior art reference to anticipate in terms of 35 U.S.C. §102, every element of the claimed invention must be identically shown in a single reference. *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 677, 7 U.S.P.Q. 2d 1315, 1317 (Fed. Cir. 1988). *See also Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). Birren does not teach every element of the claimed invention. Furthermore, Birren is not prior art to the present application under 35 U.S.C. § 102(b) because its alleged date is less than one year prior to the priority date of the present application.

1. Birren is Not Proper § 102(b) Art

The present application claims priority under 35 U.S.C. § 119 to United States Provisional Application No. 60/163,469, filed November 1, 1999, as reflected in the Amendment and Reply filed June 3, 2002. Contrary to the Examiner's assertions, the present claims are entitled to the priority date of November 1, 1999 because the prior application ***does*** disclose the

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[12] The First Advisory Action makes no reference to the rejection under 35 U.S.C. § 102 (b) and does not reiterate it as one of the bases for the rejection of the claims in this case. First Advisory Action at page 2. However, in the interest of facilitating prosecution, Applicants herein reiterate their argument directed to the rejection under 35 U.S.C. § 102(b).

nucleotide sequence recited by the claims. In particular, the nucleotide sequence enumerated as SEQ ID NO: 1 in the present application was disclosed as SEQ ID NO: 17839 in Application No. 60/163,469, so the present application ***is*** entitled to this priority date. The date relied upon by the Examiner in applying the Birren reference is November 14, 1998, which is less than one year prior to the priority date of the present application (*i.e.*, November 1, 1999). Therefore, Birren is not prior art to the present application under 35 U.S.C. § 102(b), and as such the rejection should be reversed.

Moreover, even if Applicants were not entitled to their priority date, a rejection under 35 U.S.C. § 102 (b) is only proper if, *inter alia*, an anticipatory reference is available publicly. The Examiner has submitted no evidence that Birren was available to the public prior to Applicants' priority date. The Examiner apparently relies on the date the nucleotide sequence was submitted to the GenBank database to establish the reference date under §102(b). However, there is no evidence that Birren was actually published or otherwise made available to the public at ***any*** time prior to Applicants' priority date, let alone at least one year prior to the priority date.

2. The Art of Record Fails to Anticipate Claims 1, 2 and 17-18.

Although Birren is cited for the proposition that it anticipates claims 1, 2, 17 and 18 as directed to SEQ ID NO: 1, the Examiner admits that Birren does **not** disclose the sequence of SEQ ID NO: 1. Office Action mailed September 25, 2001 (Paper Number 12), at page 10. Because the chemical disclosed in Birren is not the same as the chemical disclosed in SEQ ID NO: 1 or its complement, and does not have between 90% and 100% sequence identity with a nucleic acid molecule of SEQ ID NO: 1 or its complement, every element of the claimed invention has not been identically shown in this reference. *See Diversitech Corp.*, 850 F.2d at 677, 7 U.S.P.Q.2d at 1317. Accordingly, Birren does not anticipate claims 1, 2, and 17-18, and the rejection under 35 U.S.C. § 102(b) is improper and must be withdrawn.

The Examiner's argument is based on the alleged disclosure in Birren of a 22 base pair sequence that is 100% identical to the complement of SEQ ID NO: 1, and "a fragment of about 100 bp that is complementary to the complement of SEQ ID NO: 1". Office Action mailed September 25, 2001, at page 10. Because the Examiner asserts that "any percentage of complementarity is interpreted as a complement, and that any length of a fragment including two or more amino acid residues as a fragment of the protein", in the Examiner's opinion the alleged "complementarity" of these small fragments[13] to SEQ ID NO: 1 makes them anticipatory to the claims. *See* Office Action mailed September 25, 2001, at page 10. This argument is wrong.

First, it is axiomatic that the claims are to be read in light of the specification. *See In re Vogel*, 422 F.2d 438, 441, 164 U.S.P.Q. 619, 622 (C.C.P.A. 1970). The claim language of Claims 1, 2, 17 and 18 recites "SEQ ID NO: 1 or complement thereof", and the present specification explicitly defines the term "complement" at page 19, lines 7-10:

> A nucleic acid molecule is said to be the 'complement' of another nucleic acid molecule if they exhibit complete complementarity. As used herein, molecules are said to exhibit 'complete complementarity' when every nucleotide of one of the molecules is complementary to a nucleotide of the other.

The Examiner has not read the claims in light of the specification, as required by law, but rather has attempted to substitute a different definition of "complement" that the Examiner prefers to the explicit definition in the specification. This is impermissible.

Second, when the claims are read in light of the specification, it is clear that a nucleotide sequence cannot be the complement of SEQ ID NO: 1 unless "every nucleotide of one of the molecules is complementary to a nucleotide of the other." See specification at page 19, lines 7-10. The Examiner has not shown that ***every*** nucleotide of SEQ ID NO: 1 is complementary to a

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[13] Applicants note that Birren teaches a human chromosome segment that appears to be in excess of 29,000 base pairs in length.

nucleotide of the sequence disclosed in Birren. Therefore, Birren has not been shown to teach every element of the present invention.

The Examiner's interpretation of the word "fragment" in claim 2 is similarly flawed. The Examiner has applied an untenable interpretation of Birren to cover small fragments of the specifically claimed nucleic acid molecule, *i.e.*, molecules as short as one codon, and thus concludes that claim 2 is anticipated by Birren. Office Action mailed September 25, 2001, at page 10. A grammatically consistent interpretation of claim 2, in light of Applicants' disclosure, would require any anticipatory reference to identically show a fragment nucleic acid molecule having about 50 to about 100 nucleotide residues. Birren clearly does not disclose such a nucleic acid molecule, as it discloses only one sequence that does not have about 50 to about 100 nucleotide residues. Accordingly, Birren does not teach each and every element of claim 2 and therefore cannot anticipate claim 2.

In conclusion, even if Birren were prior art to the present invention, Birren does not expressly or inherently anticipate claims 1-2 and 17-18 because the reference does not teach SEQ ID NO: 1, or any of the other claimed nucleic acid molecules. As such, claims 1-2 and 17-18 of the present invention are not expressly or inherently anticipated by Birren, and the rejection must be withdrawn.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,

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APPENDIX A

1. A substantially purified nucleic acid molecule having a nucleic acid sequence of SEQ ID NO: 1 or complement thereof.

2. A substantially purified nucleic acid molecule comprising a fragment nucleic acid sequence having from about 50 to about 100 nucleotide residues; wherein said fragment nucleic acid sequence exhibits complete complementarity to a second nucleic acid molecule having a nucleic acid sequence of SEQ ID NO: 1 or complement thereof.

3. The substantially purified nucleic acid molecule according to claim 2, wherein said substantially purified nucleic acid molecule comprises a microsatellite sequence.

4. The substantially purified nucleic acid molecule according to claim 2, wherein said substantially purified nucleic acid molecule comprises a region having a single nucleotide polymorphism.

6. The substantially purified nucleic acid molecule according to claim 16, wherein said rice protein or fragment thereof is a homologue of a dicot plant protein or fragment thereof.

7. The substantially purified nucleic acid molecule according to claim 16, wherein said rice protein or fragment thereof is a homologue of a non-rice monocot plant protein or fragment thereof.

8. The substantially purified nucleic acid molecule according to claim 16, wherein said rice protein or fragment thereof is a homologue of a non-rice cereal protein or fragment thereof.

9. The substantially purified nucleic acid molecule according to claim 16, wherein said rice protein or fragment thereof is a homologue of a bacterial protein or fragment thereof.

16. A substantially purified nucleic acid molecule encoding a rice protein or fragment thereof from Table 1, wherein said substantially purified nucleic acid molecule comprises a fragment nucleic acid molecule having from about 50 to about 100 nucleotide residues of the nucleic acid molecule of SEQ ID NO: 1.

17. A substantially purified nucleic acid molecule having between 90% and 100% sequence identity with a nucleic acid molecule of SEQ ID NO: 1 or complement thereof.

18. The substantially purified nucleic acid molecule of claim 17, wherein said substantially purified nucleic acid molecule has between 99% and 100% sequence identity with SEQ ID NO: 1 or complement thereof.

19. The substantially purified nucleic acid molecule according to claim 17, wherein said nucleic acid molecule comprises a microsatellite sequence.

20. The substantially purified nucleic acid molecule according to claim 17, wherein said nucleic acid molecule comprises a region having a single nucleotide polymorphism.